PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32725A/USN	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/11380	International filing date *(day/month/year)* 14.10.2003	Priority date *(day/month/year)* 15.10.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/663		
Applicant NOVARTIS AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10.05.2004	13.01.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Zimmer, B Telephone No. +49 89 2399-8600

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/11380

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-18 as originally filed

Claims, Numbers

1-9 as originally filed

2. With regard to the **language,** all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1,4-9(part) with regard to industrial applicability

   because:

   ☒ the said international application, or the said claims Nos. 1,4-9(part) with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9
Industrial applicability (IA)	Yes:	Claims	2,3,4-9(part)
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1 and 4-9(part) relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 01/82903 A (LIPOCINE INC) 8 November 2001 (2001-11-08)
   D2: WO 01/97788 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH); TRECHSEL ULRICH © 27 December 2001 (2001-12-27)
   D3: KROOT ERIC-JAN J A ET AL: "Change in bone mineral density in patients with rheumatoid arthritis during the first decade of the disease" ARTHRITIS AND RHEUMATISM, vol. 44, no. 6, June 2001 (2001-06), pages 1254-1260, XP002268238 ISSN: 0004-3591

2. Novelty

   Prior art document D1 discloses the use of bisphosphonates, in particular zoledronate and pamidronate, for the preparation of a medicament for the treatment of conditions related to bone resorption such as osteoporosis and periprosthetic bone loss or osteolysis (p. 1, l. 12-17). The claimed dosage bisphosphonate preparations allow dosage regimens of most preferably once every two months and optimally every twelve weeks (p. 31, l. 21-26).
   D1 thus differs from the subject-matter of the present application in that rheumatoid arthritis is not explicitly disclosed as a disease.

   The therapeutic use of the same bisphosphonates as claimed in the present application for the treatment of abnormally increased bone turnover, such as rheuma-

toid arthritis, is known from D2 (p. 3, para. 2; p. 5 and p. 8).
In contrast to the subject-matter of the present application the administration interval of the bisphosphonate is at least 6 months (p. 3, last para. to p. 4, para. 1).

As a result, the subject-matter of independent claims 1-3 as well as dependent claims 4-9 seems to be new in view of the cited prior art (Art. 33(2) PCT).

3. Inventive Step

Although the subject-matter of the present application seems to be new in view of the cited prior art it does not involve an inventive step for the following reasons:

3.1 D1, which is regarded as closest prior art, differs from the subject-matter of the present application in the lack of the specific disclosure of rheumatoid arthritis (see above).
Thus, in view of the cited prior art the technical problem of the present application seems to be the provision of a new therapeutic use of a bisphosphonate with a period between administrations of bisphosphonates from at least 2 months up to 4 months.
As it is already known from D1 that this dosage regimen for bisphosphonates is used for the treatment of osteoporosis and further from D3 (p. 1254, right col., para. 3) that osteoporosis is frequently observed in patients with rheumatoid arthritis, it is obvious for a person skilled in the art to combine the teachings of both documents and arrive at the subject-matter of the present application (Art. 33(3) PCT).

3.2 Starting from D2 as closest prior art the technical problem of the present application would be the provision of an alternative dosage regimen of bisphosphonates for the treatment of rheumatoid arthritis.
As periods of administration of bisphosphonates from 2 to 3 months are disclosed in D1 (see above) a person skilled in the art would combine D1 and D2 and arrive at the subject-matter of the present application.

3.3 Dependent claims 4-9 do not appear to contain any additional features which involve an inventive step when combined with the subject-matter of any claim to which they refer. Dependent claims are only allowable when related to a patentable independent claim (Rule 6.4 PCT).

4. Further remarks

4.1 Claims 4-9 of the present application relate to different types of claims, i.e. product claims, method claims and use claims, which leads to an unclarity (Art. 6 PCT). This objection could be overcome by dividing said claims into dependent claims of one category each.

4.2 The term "about" used in the independent and dependent claims is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of the claims unclear (Art. 6 PCT).

5. For the assessment of the present independent claim 1 as well as claims 4-9 with regard to the method on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.